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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/502,538	07/28/2004	Laurent Francois Andre Hennequin	056291-5172	7795

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MORGAN LEWIS & BOCKIUS LLP
1111 PENNSYLVANIA AVENUE NW
WASHINGTON, DC 20004

EXAMINER

TRUONG, TAMTHOM NGO

ART UNIT	PAPER NUMBER
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1624

DATE MAILED: 03/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/502,538

Applicant(s)HENNEQUIN, LAURENT
FRANCOIS ANDRE**Examiner**

Tamthom N. Truong

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-26 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-26 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 7-20-04.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: ____.

DETAILED ACTION

Claims 1-26 are pending.

Priority

1. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-13, 18-22, 25 and 26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

- a. The limitations within parentheses are not clear whether or not they are part of the claims.
- b. In the definition of R⁵, groups 2-4, 6-8, 10-17, 20-22 are unclear as to where the point of attachment is. For example, the group "C₁₋₅alkylX²C(O)R¹¹" (in group 2), would it attach to the quinazolinyl ring through the alkyl group or through R¹¹? Likewise, it is unclear how groups 3, 4, 6-8, 10-17 and 20-22 are attached to the quinazolinyl ring.

c. Also, in the same definition, group 9 recites “pyridone” which is a narrow limitation followed by the broad limitation of “5-6-membered aromatic heterocyclic group...”. It is unclear which limitation is intended for R⁸⁰.

d. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by “such as” and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949).

e. In the definition of Q¹, it is unclear how groups 2-10 are attached to ring C or the quinazolinyl ring. That is, would those groups attach to said rings through the alkyl group or through Q², or Q¹⁴ (for group 9), or Q^{14a} (for group 10).

f. In claim 1, the phrase “or R¹ can be selected from any of the groups defined herein” has indefinite metes and bounds because R¹ can be a monvalent group represented by ring C, R⁵, R²⁸, R²⁹, R⁵⁴, or R⁵⁵, etc. as well as a divalent group

represented by Z, X¹, W³, W⁴, etc. Furthermore, the scope of anyone of the variables is not the same, and thus, it is unclear what the intended scope for R¹ is.

g. The limitation of R² as “6,7-methylenedioxy or 6,7-ethylenedioxy” is not clear unless two of R² form such a ring. If one R² has two dioxy groups, then there will be an incomplete valence. Clarification is solicited.

h. Claim 2 lacks antecedent basis for reciting R^{1a} as an “oxo” group, which is not recited in claim 1.

i. Claim 19 lacks antecedent basis for reciting R⁵ as “C₁₋₅alkylR¹¹³”, which is not recited in claim 1. Many variables such as R¹¹⁴, R¹¹⁵, R¹¹⁶-R¹²⁰, R¹²⁷, R¹²⁸, etc. are not recited in claim 1 either.

j. Claim 21 provides for the use of “a compound according to claim 1, claim 2 or claim 5”, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

k. Claim 22 recites a “method for producing an antiangiogenic and/or vascular permeability” which has indefinite metes and bounds because it is unclear what disease is treated (i.e., hypertension or cancer?).

l. Claims 5, 25 and 26 recite the term “azaindole” which has indefinite metes and bounds because it is not clear what the maximum number of ring nitrogen is, or their

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locations. Without a structure, it is unclear as to what the arrangement of the ring atoms is.

m. Claims 2-13 and 18-22 are (also) rejected as being dependent on claim 1 and carrying over indefinite limitations.

Claim Rejections - 35 USC § 101

3. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Use Claim: Claim 21 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Double Patenting

The **nonstatutory double patenting** rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

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provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 1-4, 10 and 18-22 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-16 and 21-24 of copending Application No. **10/494,137**. Although the conflicting claims are not identical, they are not patentably distinct from each other when the Formula I of the copending application has the following substituents:

- i. Q^2 is formula Ib, Ic, Id, or Ie (which corresponds to the instant ring C);
- ii. Q^1-Z corresponds to the instant R^2 when it is Q^1X^1- ;
- iii. R^1N- corresponds to the instant Z when it is $-NH-$;
- iv. $m = 1$, and R^2 can be anywhere on the benzo ring including the 5th position;

Formula I of the copending application only differs from the instant Formula I by having a narrower scope with the substituent Q^1-Z at the 5th position only. However, it would have been within the level of the skilled chemist to recognize that Formula I of the copending application is but a subgenus of the instant Formula I. Therefore, it would have been obvious it would have been obvious to make and use the instant Formula I in view of the claims in the copending application.

5. Claims 1-4, 10 and 18-22 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-19 and 22-25 of

copending Application No. **10/494,388**. Although the conflicting claims are not identical, they are not patentably distinct from each other when the Formula I of the copending application has the following substituents:

- v. $m = 0$, and thus, R^1 does not exist, which means the benzo ring only has Q^1-Z as a substituent;
- vi. Q^1-Z corresponds to the instant R^2 when it is Q^1-X^1 ;
- vii. R^2 is hydrogen;
- viii. L is a direct bond;
- ix. R^3N- corresponds to the instant Z when it is $-NH-$;
- x. Q^2 is formula Ia with G^3 and G^4 together forming $-CH=CH-NH-$, $-NH-CH=CH-$, $-NH-N=CH-$, $-CH=N-NH-$, etc. (Q^2 corresponds to the instant ring C).

The Formula I of the copending application only differs from the instant Formula I by having a narrower scope with the substituent Q^1-Z at the 5th position only. However, such a difference would have been within the level of the skilled chemist to recognize that the Formula I of the copending application is only a subgenus of the instant Formula I. Therefore, it would have been obvious to make and use the instant Formula I in view of the claims in the copending application.

6. Claims 1, 4, and 18-22 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-17 of copending Application No. **10/344,678**. Although the conflicting claims are not identical, they are not

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patentably distinct from each other when the Formula I of the copending application has the following substituents:

- xi. R^1 is a group of Q^1-X^1 which corresponds to the instant R^2 when it is Q^1-X^1 ;
- xii. R^2N- corresponds to the instant Z when it is $-NH-$;
- xiii. The ring '*benzomethylenedioxy*' corresponds to the instant ring C.

The Formula I of the copending application only differs from the instant Formula I by having a narrower scope with the ring *benzomethylenedioxy* attached to the amino group R^2N- . However, such a difference would have been within the level of the skilled chemist to recognize that the Formula I of the copending application is only a subgenus of the instant Formula I. Therefore, it would have been obvious to make and use the instant Formula I in view of the claims in the copending application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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7. Claims 1-10 and 18-22 are rejected under 35 U.S.C. 102(b) as being anticipated by **Hennequin et. al.** (WO 00/47212).

On pages 54-58, Hennequin et. al. disclose several quinazoline compounds that are substituted with *indolyl-oxy* at the 4th position, and also substituted with a group such as: 3-(*pyrrolidin-1-yl*)propoxy or 3-(*piperidinopropoxy*), etc. (e.g., see compounds on lines 31 & 31 on page 57). Also, on page 115, Table I lists compounds #25, 26 which are quinazoline substituted with *indazolyl-amino*;

The disclosed compounds read on the instant Formula I when it has the following substituents:

- Z is -O-, -NH-;
- Ring C is indolyl or indazolyl;
- m = 2;
- one of R² is methoxy, and the other is Q¹-X¹;
- X¹ is -O-;
- Q¹ is C₁₋₅alkylQ²;
- Q² is a 5- or 6-membered saturated or partially saturated heterocyclic group with 1-2 heteroatoms.

The disclosed compounds also reduce antiangiogenic effect or vascular permeability.

The process for making said compounds in WO'212 also reads on the process in the instant claim 19 because the same intermediates are used (see pages 66-79). For example, the

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disclosed Formula (III) corresponds to the instant Formula (III), and the disclosed Formula (IV) corresponds to the instant Formula (IV), etc.

Thus, the teaching of Hennequin et. al. completely anticipates the above claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 5-13, 14-17, 23 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Hennequin et. al.** (WO'212).

The instant claims 5-13 recite quinazoline compounds having ring C as an "azaindolyl". Although there is no species in WO'212 has such a ring, on page 12, Hennequin describes a preferred embodiment for ring C which includes a "*9-10-membered heteroaromatic bicyclic moiety which contains 1 or 2 nitrogen atoms.*" Such a teaching would have motivated one skilled in the art to select the instant azaindole as ring C since it met the description of the preferred embodiment.

The instant claims 14-17, 23 and 24 recite species of quinazoline compounds with indolyl-oxy and a substituent such as: *(4-acetylpiperazin-1-yl)propoxy*; *benzyloxy*; or *hydroxyl*.

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Although WO'212 does not appear to disclose said species, the definition of R^2 allows for such a substituent (e.g, page 3, line 19 (for hydroxyl), line 21 (for R^5X^1), etc.).

Since Hennequin's compounds have the same activity, one of the ordinary skill in the art would have been motivated to select the instant species from the genus in WO'212 because said compounds would have expected to reduce antiangiogenic effect and/or vascular permeability as well.

Therefore, at the time of the invention, it would have been obvious to make and use species claimed herein in view of the teaching above.

No pending claims are allowed.

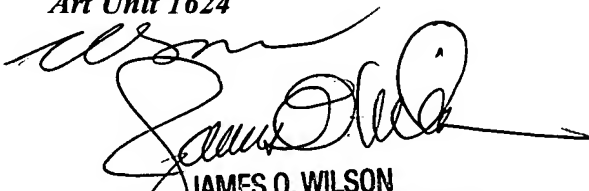
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tamthom N. Truong whose telephone number is 571-272-0676. The examiner can normally be reached on M-F (10:00-6:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Tamthom N. Truong
Examiner
Art Unit 1624

3-17-05


JAMES O. WILSON
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600